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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Reed Smith LLP
East Tower - Suite 1100
1301 K Street, N.W.
Washington, DC 20005-3373

EXAMINER	
HUMPHREY, LOUISE WANG ZHIYING	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 03/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/770,467	PLACHTER, BODO	
	Examiner	Art Unit	
	Louise Humphrey, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-23 and 25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-18, 20-23 and 25* is/are rejected.

7)☒ Claim(s) *15 and 19* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/914,948.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's Preliminary Amendment, filed 4 February 2004, is acknowledged. Claims 1-14 and 24 have been canceled. Claim 25 has been added. *Claims 15-23 and 25 are pending.*

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. §119(a)-(d), which papers have been entered. Applicant's provision of foreign priority documents, GERMANY 19910044.6, in the parent application 09/914,948, is acknowledged.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specification

Applicant is required to update the status (pending, allowed, etc.) of all parent priority applications in the first line of the specification. The status of all citations of US filed applications in the specification should also be updated where appropriate. In the

instant case, Applicant is required to state that the parent application 09/914,948 has been issued a patent, US 6,713,070.

The disclosure is objected to because of the following informalities: the title on page 1 is missing an "e" in the word "released".

Appropriate correction is required.

The use of the trademark FuGENE transfection reagent has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

Claim 15 and 19 are objected to because of the following informalities:

Independent claim 15 recites "HCMV" without first defining the term. A claim should recite the full name, followed by the acronym to avoid any confusion.

Claim 19 is objected to for depending from rejected claims.

Appropriate correction is required.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 15, 18, and 20 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 18 recites a trademark or trade name as a limitation to identify or describe the transfected mammalian cells. See M.P.E.P. §2173.05(u). *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. In fact, the value of a trademark would be lost to the extent that it became descriptive of a product, rather than used as an identification of a source or origin of a product. Thus, the use of a trademark or trade name in a claim to identify or describe a material or product would not only render a claim indefinite, but would also constitute an improper use of the trademark or trade name.

Claims 15 and 20 are rejected under 35 U.S.C. §112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: infection of missing-gene-transfected mammalian cells with HCMV with deleted genome.

Clarification and/or correction are required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 21, 23, and 25 are rejected under 35 U.S.C. §102(b) as being anticipated by Gibson *et al.* (1984).

The instant claims read on viral particles, which are released after infection of mammalian cells by HCMBV, and pharmaceutically acceptable carrier for formulation into a composition for immunization against HCMV diseases and infections.

Gibson teaches the isolation of dense bodies (DBs) and noninfectious enveloped particles (NIEPs) after infection of mammalian cells by HCMV, and their use as HCMV subunit vaccine candidates (page 306, Noninfectious HCMV Particles Are Subunit Vaccine Candidates). Gibson further teaches that neither DBs nor NIEPs contain DNA but both contain all glycoprotein species present in virions, and that DBs lack all of the capsids (page 321, Summary). Thus, the instant invention is anticipated by Gibson.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 15 and 16 are rejected under 35 U.S.C. §103(a) as being unpatentable over Michel *et al.* (1996) in view of Wang *et al.* (US 5,830,727).

The instant invention is a method for replicating HCMV comprising the provision of an HCMV in whose genome an essential gene has been deleted, the provision of a

stably transfected human foreskin fibroblast cell line which expresses the deleted HCMV gene, and replication of the deleted virus in the cell line.

Michel *et al.* discloses an HCMV gene with the N-terminal region of UL97 deleted. The deleted HCMV is replicated in human foreskin fibroblasts. See page 6340, Materials and Methods.

Michel *et al.* does not disclose transfected mammalian cell line which expresses the deleted HCMV gene so that the deleted HCMV can replicate in the cells.

Wang *et al.* discloses the technique of isolation and propagation of deletion mutant Herpes Simplex Viruses in a cell line transfected with complementing levels of the deleted essential gene of the viruses. Column 6, lines 33-51. Column 7, lines 14-39.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to add the cell line transfected with complementing levels of deleted essential viral gene of Wang *et al.* to the methods of Michel *et al.* to improve the efficiency of HCMV replication. One having ordinary skill in the art would have been motivated to do this so that the replication-deficient viruses with deleted essential genes can replicate in a mammalian cell, which will help make replication-incompetent viruses delivering therapeutic genes inserted into deleted regions in the viral genome, per the suggestion in Wang *et al.*, with a reasonable expectation of success because the working example of Wang *et al.* is HSV, which is in the same family as HCMV. Thus, claims 15 and 16 are obvious over Michel *et al.* in view of Wang *et al.*

Claims 15, 17, and 18 are rejected under 35 U.S.C. §103(a) as being unpatentable over Michel *et al.* (1996) in view of Wang *et al.* (US 5,830,727), and further in view of Uyttersprot *et al.* (1998).

The instant invention is further limited to transfecting mammalian cells with a lipid-containing reagent.

The relevance of Michel *et al.* and Wang *et al.* are set forth above. Michel *et al.* and Wang *et al.* do not disclose the method step of cell transfection with a lipid-containing reagent.

Uyttersprot *et al.* discloses the lipid formulation, FuGENE 6 transfection reagent. See entire document.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to add the FuGENE transfection reagent of Uyttersprot *et al.* to the combined methods of Michel *et al.* and Wang *et al.* to improve the efficiency of HCMV replication. One having ordinary skill in the art would have been motivated to do this so that mammalian cell transfection has increased uptake, as per the suggestion in Uyttersprot *et al.*, which will increase the yield of viruses with a reasonable expectation of success because Uyttersprot *et al.* specifically states successful transfection of human foreskin keratinocytes using the FuGENE 6 transfection reagent. Thus, claims 15, 17, and 18 are obvious over Michel *et al.* in view of Wang *et al.*, and further in view of Uyttersprot *et al.*

Claim 20 is rejected under 35 U.S.C. §103(a) as being unpatentable over Michel *et al.* (1996) in view of Wang *et al.* (US 5,830,727), and further in view of Irmiere *et al.* (1983).

The instant invention is directed to a method for producing viral particles comprising the following steps: a) provision of HCMV as set forth in any of claims 15-19, b) infection of mammalian cells with virus which has been replicated as in step (a), (c) isolation of viral particles from cells which have been infected as in step b), wherein (d) the particles are surrounded by a lipid membrane in which viral glycoproteins are embedded, (e) the particles contain neither viral DNA nor capsids.

The relevance of Michel *et al.* and Wang *et al.* are set forth above. Michel *et al.* and Wang *et al.* do not disclose the method step of isolation of HCMV viral particles from infected cells.

Irmiere *et al.* discloses isolation and characterization of noninfectious virion-like particles from human foreskin fibroblast cells. See pages 119-120, Materials and Methods, particle purification). Irmiere *et al.* specifically discloses that the dense bodies contain neither viral DNA nor capsids. See page 123, left column, first paragraph.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to add the combined methods of Michel *et al.* and Wang *et al.*, to the method step of isolation of viral particles, as taught by Irmiere *et al.* to ensure the non-infectivity of HCMV viral particles. One having ordinary skill in the art would have been motivated to do this so that the viral particles prepared by the combined method has increased safety, as per the suggestion in Wang *et al.* Thus,

claim 20 is obvious over Michel *et al.* in view of Wang *et al.*, and further in view of Irmiere *et al.*

Claims 21 and 22 are rejected under 35 U.S.C. §103(a) as being unpatentable over Gibson *et al.* (1984) in view of Wills *et al.* (1996).

The instant invention is directed to a composition comprising sub-viral particles that contain a fusion protein comprising one or more parts of the T-cell antigen pp65 (UL83) and one or more parts of one or more proteins that are not pp65.

The relevance of Gibson *et al.* is set forth above. Gibson *et al.* does not expressly disclose the fusion protein of pp65 and other proteins.

Wills *et al.* discloses pp65 and other proteins as specific CTL epitopes. See page 7571, Figure 1.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to modify the viral particles of Gibson *et al.* by the addition of pp65-IE1 fusion protein of Wills *et al.* to increase the immunogenicity of the composition with a reasonable expectation of success. One having ordinary skill in the art would have been motivated to do this so that the viral particles have increased immunogenicity, such as CTL immune responses elicited by pp65 and IE1, as suggested by Wills *et al.* Thus, claims 21 and 22 are obvious over Gibson *et al.* in view of Wills *et al.*

Allowable Subject Matter

Claim 19 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Claim 19 is apparently free of prior art of record. The close prior art, Michel *et al.* does not teach or fairly suggest deletion of the major capsids protein gene (UL86) from the HCMV genome.

Remarks

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, Ph.D., whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Louise Humphrey, Ph.D.
Patent Examiner
10 January 2006

JEFFREY STUCKER
PRIMARY EXAMINER